SUPPORT FOR THE AMENDMENTS

Claims 1 and 4 were previously canceled.

Claims 2, 8, and 9 have been amended.

Support for the amendment of Claims 2, 8, and 9 is provided by the \ specification at, for example, paragraphs [0012] to [0014].

No new matter has been added by the present amendments.

REMARKS

Claims 2-29 are pending in the present application.

Applicants wish to thank Examiner Sutton and Examiner Lundgren for the helpful and courteous discussion with their undersigned Representative on November 5, 2009. During this discussion, various arguments (including those presented herein) were discussed. The content of this discussion is believed to be accurately reflected by the amendments and comments presented herein. Reconsideration of the outstanding rejections is requested in view of the amendments and remarks herein.

The rejections of:

(a) Claims 2, 3, 5-7, 9, 12, 13, and 26-29 under 35 U.S.C. §103(a) over Winston et al (US 5,858,333) in view of Usen et al (US 5,605,675) and Tomlinson et al (US 4,048,300);

(b) Claims 14-17 and 21 under 35 U.S.C. §103(a) over Winston et al (US 5,858,333) in view of Usen et al (US 5,605,675) and Tomlinson et al (US 4,048,300) and further in view of Grabenstetter et al (US 4,083,955); and

(c) Claims 8, 10, 11, 18-20, and 22-25 under 35 U.S.C. §103(a) over Winston et al (US 5,858,333) in view of Usen et al (US 5,605,675) and Tomlinson et al (US 4,048,300) and further in view of Wiesel (US 6,287,120) and Grabenstetter et al (US 4,083,955),

are respectfully traversed.

In the outstanding Office Action the Examiner essentially restates the previous rejections centered on the combined disclosures of Winston et al (WO 1998/13012) and

Tomlinson et al (US 4,048,300). The Examiner now "adds" Usen et al (US 5,605,675) to this combination of references, but this reference was already relied upon in the same manner in the Office Action mailed October 31, 2008 (see footnote on page 3). Thus, the rejections raised by the Examiner are not new and the references are not applied in any way that was not previously made of record.

This is important in this case as Applicants have already responded to the Examiner's allegations related to the current rejections in the response filed on February 26, 2009, which was accompanied by a Declaration under 37 C.F.R. §1.132 ("the first Yamagishi Declaration"). When filing the RCE on April 30, 2009, entry of this response was requested for further consideration by the Examiner. The Examiner makes no attempt to address the response filed on February 26, 2009 and/or the first Yamagishi Declaration and the rejection based on the combined disclosures of Winston et al, Usen et al, and Tomlinson et al have not been modified to address or rebut any argument that we made.

The Examiner's treatment of this application is contrary to proper examination procedure as set forth in MPEP §707.07(f), which requires: "Where the applicant traverses any rejection, the examiner should, if he or she repeats the rejection, take note of the applicant's argument and answer the substance of it." Clearly the Examiner has failed to meet this obligation.

Nonetheless, in the Advisory Action mailed April 24, 2009, the Examiner did provide a specific criticism of the first Yamagishi Declaration. In particular, the Examiner alleged that the table in Declaration "does not probatively show the claimed superior fluoride uptake because the experimental design does not compare equivalent compositions. Applicant has compared an example from the Winston et al prior art alone to compositions of the instant application. Winston et al teach, however, that monofluorophosphate can be incorporated

into the second component with the calcium compound and therefore comparisons to compositions that do contain monofluorophosphate within the calcium component would have been more representative of the closest prior art." Applicants submit that this allegation by the Examiner is without merit.

Specifically, the first Yamagishi Declaration reveals the fluoride uptake of the composition containing monofluorophosphate in Winston et al's composition in the Comparative Example B2 as well as Winston et al's composition, i.e., the Comparative Example B1. Applicants submit that Comparative Example B2 shows the comparison to the composition as stated in the Advisory Action.

Indeed, the labels as "part A" and "Part B" described in the first Yamagishi Declaration adopt those in Winston et al (US 5,858,333 and WO1998/13012), which direct to a second composition (B) and a first composition (A) in the present invention, respectively. In fact, the preset invention reverses the wording "A" and "B" with respect to Winston et al. Rather than focusing on the label applied to the individual compositions, it is necessary to actually look at the components in the individual compositions.

In the composition of the Comparative Example B1, B2 and B3, Part A contains calcium component. Moreover, the Part A of the Comparative Example B2 includes monofluorophosphate and thus it is believe to represent a comparison that the Examiner appears to allege is lacking in Advisory Action. It is further noted that Winston et al do not disclose any example in which Part A contains both monofluorophosphate and calcium component.

Winston et al describe two composition A and B are mixed and then applied. Therefore, monofluorophosphate is added to Part A containing calcium component in Winston et al to thereby immediately precipitate calcium phosphate. It is clear from

Comparative Example B2 that adding monofluorophosphate to calcium-containing Part A, i.e., mixing Part A and B in Winston et al, is not effective for fluorine uptake.

Both Winston et al and Usen et al disclose the Part A and B are mixed and then applied and therefore monofluoro -phosphate is added to the Part A containing calcium to thereby decrease an uptake amount of fluorine. The skilled artisan would not expect to attain excellent fluorine uptake by alternately applying the separate Part A and B in which Part A contains monofluorophosphate based on Winston et al. Winston et al is silent about claimed composition of Part A and Part B and alternately applying of them.

Tomlinson et al discloses the alternately apply of the composition, but merely describe monofluorophosphate as one of fluorides and is silent about calcium salts of polyol phosphate. Accordingly, the skilled artisan would not expect the claimed compositions Part A and B or alternately applying thereof to thereby maximum fluorine uptake. None of the cited references disclose when monofluorophosphate is contained in the composition, fluorine uptake can be attain only by alternately applying of the composition Part A and B.

This error in treatment of the first Yamagishi Declaration and the foregoing argument was brought to the Examiner's attention during the interview on November 5, 2009. In the Interview Summary, the Examiner makes a new attempt to disregard the evidence of record as being irrelevant and not to "represent a fair comparison between the claimed composition and the closest prior art." The Examiner's new position is that:

> "While the pH of the individual A and B components of Applicants' composition are provided, Applicants do NOT disclose the individual pH of the A and B components of the comparative examples. Accordingly, one of ordinary skill in the art could not determine from Applicants Declaration whether or not there exists an unexpected result from the combination of MFP and the claimed calcium salt of polyol phosphate. Therefore, based on the art of record, Applicants have not demonstrated that the calcium sources of the prior art references are equivalent when used with MFP."

With this in mind, the Examiner continues to allege that Applicants have failed to give Tomlinson et al fair consideration as relied upon. In this regard, the Examiner states:

> "Tomlinson, as referenced in the Non-final rejection, dated 07/23/2009, page 9, shows that fluctuating the pH of a dual component composition between about 4 to about 7 provides optimum incorporation of fluoride ions, i.e. fluoride uptake. Therefore, the pH of each component in the composition is a very important variable when alternately applying each component to the teeth when optimum uptake of fluoride is desired. Since the Declaration does not provide data on the pH of each component, i.e. A and B, of the comparative examples it is not possible to compare them to the instant invention and to assess the alleged unexpected results.
>
> Moreover, independent claim 9 does not require a particular pH for components A and B. Therefore, by not holding the pH of the comparative examples the same as the "claimed" example, the results are not comensurate in scope with the claim."

Applicants disagree with these new allegations raised by the Examiner in a belated attempt to remedy the procedural errors in the Office Action mailed July 23, 2009, and the failure to properly consider the first Yamagishi Declaration. Nonetheless, to further illustrate the non-obviousness of the presently claimed invention, Applicants **submit herewith** a second Yamagishi Declaration.

In the second Yamagishi Declaration, the experiment provided in the first Yamagishi Declaration has been updated to include the pH of the individual compositions (i.e., part A and part B; see Table 1). In addition, the Yamagishi Declaration provides two new experiments (see paragraphs 11-16).

As previously established in the response filed on July 15, 2008 and February 26, 2009, Winston et al fail to disclose or suggest alternately applying a first composition (A) and a second composition (B) to a tooth where the first composition (A) contains a fluoride ion-supplying compound and an inorganic phosphoric acid or a salt thereof; and the second composition (B) contains a calcium salt of organic acid, wherein an organic acid constituting

the calcium salt of organic acid has a pKa value ranging from 3 to 11, or at least one pKa value ranging from 3 to 11 when the organic acid has plural pKa values.

Winston et al disclose one-part or two-part products for remineralizing or mineralizing teeth (see Abstract). However, throughout the specification, Winston et al disclose that "when the product... is ready to be used, the cationic and anionic components are mixed together with water and/or saliva to form the mixed aqueous composition... The anionic and cationic components are mixed only when the components are introduced into the oral cavity or immediately before their introduction into the oral cavity" (see page 23, line 29 to page 24, line 6). Further, at page 36, lines 11-29, Winston et al specifically disclose "When using the two-part aqueous products of this invention, the time period between the mixing of the first and second parts and the application of the resulting mixed aqueous composition to the teeth should not exceed 1 minute.... An important feature of the present invention lies in the mixing of the anionic and cationic components and the quick and timely application of the resulting mixed composition to the tooth..."

In view of the foregoing and the remainder of the disclosure by Winston et al, including the Examples, it is clear that the two-part system disclosed therein is either mixed simultaneously (at best in the oral cavity as opposed to on the tooth surface) or pre-mixed before application to the oral cavity or teeth. In contrast, the claimed invention requires the alternate application of composition (A) and composition (B). The meaning of "alternate application" is clear from the disclosure of the present application and means that either composition (A) or composition (B) is applied to the teeth followed after a certain time interval the application of the other composition (see, for example, paragraphs [0011], [0019], and [0032]-[0034], and the Examples). Winston et al does not disclose or suggest the alternate application as claimed.

The foregoing distinction is important for two reasons. First, the fact that Winston et al does not disclose or suggest the alternate application as claimed means that this reference cannot anticipate the claimed invention. Second, Applicants submit that the claimed method provides a substantial unexpected advantage with respect to fluorine uptake as compared to either simultaneously applying (A) and (B) or pre-mixing (A) and (B) prior to application, each of which is more representative of the disclosure of Winston et al.

In the Office Action mailed October 31, 2008, the Examiner acknowledged that Winston et al fails to disclose the method of alternately applying the separate compositions. In an attempt to compensate for this deficiency, the Examiner cites Tomlinson et al, which Applicants submit does not.

Winston et al disclose a two-part product containing a cationic part and an anionic part. The anionic part may contain at least one water-soluble fluoride salt. These salts are preferably present in the anionic part rather than in the cationic part so as to avoid formation of sparingly soluble calcium fluoride (see, column 8, lines 53-59). Although the cationic part may contain MFP (monofluorophosphate) with calcium salt, Winston et al specifically disclose that inclusion of MFP in the cationic part is less desirable due to the potential loss of fluoride (see, column 9, lines 17-21).

Therefore, Winston et al discloses the product which includes a cationic part containing calcium supplier and an anionic part containing sodium fluoride and MFP, while the reference does not specifically disclose a product including fluoride in both parts or a product including both MFP and calcium salt in one part, but rather discloses that such a product would not be desirable and/or would be expected to have poor fluorine uptake proprieties.

Example 12 of Tomlinson et al do not include a calcium salt of polyol phosphate or organic acid. The product of Tomlinson et al also do not contain fluoride in both parts. Additionally; in the second solution of Example 12 of Tomlinson et al, calcium phosphate should be immediately precipitated and only a very small amount of calcium remains in supernatant. The specification of Tomlinson et al does not provide any further clarity with respect to the specific ingredients of the compositions making up the claimed product. And thus, fails to compensate for the deficiencies in Winston et al.

In contrast to Winston et al, the claimed two-part product includes composition (A) containing an inorganic fluoride and composition (B) containing MFP and calcium salt of polyol phosphate, which thus includes fluoride in both parts and contains both MFP and calcium salt in one part. To demonstrate the unexpected results flowing from the claimed invention as compared to the stated expectation in Winston et al, Applicants again point to the first Yamagishi Declaration and the explanation of the probative value of this declaration provided above. Applicants further direct the Examiner's attention to the second Yamagishi Declaration, in which the declarant again reports on a comparison of the claimed product to Example 5 of Winston, which, of the Examples, provides the highest increase in hardness (see Table VII).

As shown in Table 1 of the second Yamagishi Declaration, the amount of fluorine uptake derived from the claimed product was nearly three times larger (2.00 $\mu g/cm^2$ vs. 0.75 $\mu g/cm^2$) than that derived from Comparative Example B1 (Example 5 composition of US 5,858,333 ("Winston")). Comparing with the Comparative Example B2, which is the Example 5 composition of Winston further containing MFP in Part A, the claimed product resulted in more than two-fold fluorine uptake (2.00 $\mu g/cm^2$ vs. 0.82 $\mu g/cm^2$). In Comparative Example B3, in which MFP was contained in Part A as the only fluorine

supplier, fluorine uptake was poor (0.05). (see paragraph 7 of the second Yamagishi Declaration)

On the basis of these data, the declarant of the Yamagishi Declaration states:

> Winston disclose that the cationic part (i.e., Part A) may contain MFP (monofluorophosphate) with calcium salt, but it is less desirable due to the potential loss of fluoride (see, column 9, lines 17-21). As a result, Winston does not provide any Examples in which MFP is used. Thus, based on the disclosure of Winston, the artisan would have expected that the presence of MFP in the cationic part (i.e., Part A) would result in the loss of fluoride and would be dissuaded from using MFP in this part. Indeed, as illustrated in Comparative Example B2 above, adding MFP to part A of Example 5 of Winston resulted in poor fluorine uptake.
>
> In contrast to the expectation presented by the disclosure of Winston, the claimed product, which includes MFP with calcium salt (i.e., in Part A), leads to excellent fluoride uptake rather than resulting in loss of fluoride (see, Table 1 above). Such excellent fluoride uptake (i.e., two-fold over Winston's composition with MFP in Part A and nearly three-fold of Winston's exemplified composition) provided by the claimed invention is in no way expected from the disclosure of Winston.
>
> This result is also unexpected even when considering the disclosures of US 4,048,300 (Tomlinson), US 4,083,955 (Grabenstetter), and/or US 6,287,120 (Wiesel). This conclusion remains true even when considering newly cited US 5,605,675 (Usen et al). (see paragraph 9 of the second Yamagishi Declaration)

The Examiner is reminded that "[a] prima facie case of obviousness ... is rebuttable by proof that the claimed compounds possess unexpectedly advantageous or superior properties." *See* MPEP §2144.09 (citing *In re Paesch*, 315 F.2d 381 (C.C.P.A. 1963)). Applicants submit that the results summarized above and provided in the second Yamagishi Declaration establish that the claimed dental product possesses unexpected advantages and superior properties as compared to the products disclosed in Winston et al, even when viewed with Tomlinson et al, Usen et al, Grabenstetter et al and Wiesel.

The Examiner is further reminded of the fact that Winston et al fail to disclose the alternate application of the two compositions of the presently claimed invention. The advantages of the same were demonstrated in the Declaration under 37 C.F.R. §1.132

submitted on July 15, 2008 ("the July 15, 2008 Declaration"). In the July 15, 2008 Declaration, Applicants showed the following comparison of the results obtained as a measure of fluorine uptake ($\mu g/cm^2$) for the claimed method and two methods that are representative of the disclosure of Winston et al:

	Alternately applying (A) and (B)[i]		Simultaneously applying (A) and (B)[ii]		Pre-mixing (A) and (B)[iii]	
	1 min.	3 min.	1 min.	3 min.	1 min.	3 min.
Example 1	5.2	13.5	0.3	0.4	0.1	0.2
Example 2	5.8	15.8	0.6	0.6	0.2	0.2
Example 3	4.9	11.5	0.8	0.9	0.3	0.4
Example 4	0.6	5.2	0.2	0.2	0.1	0.1
Example 5	0.3	3.8	0.1	0.1	0.1	0.1

i) Alternately applying (A) and (B): alternately at 10 second intervals
ii) Simultaneously applying (A) and (B): mixed at teeth
iii) Pre-mixing (A) and (B): pre-mixed for 10 seconds prior to application to teeth

These results clearly evidence the unexpected superiority of the claimed method with respect to fluorine uptake is demonstrated as compared to method representing the disclosure of Winston et al, even when viewed with Tomlinson et al, which further rebuts the alleged obviousness rejection.

Applicants now take the demonstration of unexpected results one step further. In the second Yamagishi Declaration, the Declarant provides two additional experiments.

In the first experiment appearing in paragraphs 11-13 of the second Yamagishi Declaration, a comparative experiment suggested by the Examiner in the Interview Summary dated November 5, 2009, was performed. Specifically, each pH of Composition A and B was

adjusted to be same as those of examples in the claimed invention. The pH values of each mixed solution were shown in Table 3 since pH values would have an effect on a production of a salt of calcium phosphate.

The experimental result in Table 4 show that fluorine uptake amount of Comparative Examples C1 and C2 could be increased since each pH thereof was very low. However, it was also clearly shown that HAP pellets were apparently melted because of their low pH. Thus, the effect of monofluorophosphate could not be compared since a salt of calcium phosphate was not produced. (see paragraph 13 of the second Yamagishi Declaration)

Since the HAP pellets were melted in the experiment appearing in paragraphs 11-13 of the second Yamagishi Declaration, the declarant investigated the buffering capacity of the mixed solution of Compositions A and B (se paragraphs 14-16 of the second Yamagishi Declaration). In these experiments a solution containing calcium nitrate, calcium lactate or calcium glycerophosphate was added to an acidic solution of sodium fluoride containing phosphate (pH 3.7) and each pH was measured. The results for these experiments are illustrated in Table 5 and Figure 1 of the second Yamagishi Declaration.

In paragraph 17 of the second Yamagishi Declaration, the declarant sets forth the relevance of the newly added experimental data stating:

> In accordance with the foregoing experimental results, the mixed solution has low pH in Comparative Examples C1 and C2 because its buffering capacity of calcium salts included therein and therefore teeth would not be repaired, but melted. In addition, Comparative Examples C1 and C2 do not show the effect of the claimed invention, which effects are to increase production of a salt of calcium phosphate and to increase fluorine uptake.
>
> This result is also unexpected even when considering the disclosures of US 4,048,300 (Tomlinson), US 4,083,955 (Grabenstetter), and/or US 6,287,120 (Wiesel). This conclusion remains true even when considering newly cited US 5,605,675 (Usen et al).

Moreover, Applicants submit that in the presently claimed invention, the product of the present invention has the composition A having pH of 2 to 6 and composition B having pH of 6 to 12 and alternately applied to teeth, to thereby promptly form a calcium phosphate on teeth and enables uptake of fluorine.

On the other hand, Winston et al uses calcium nitrate and calcium lactate and these calcium salts have a an acid with pKa of less than 3, about 1, and they have no buffering capacity. Accordingly, when the compositions A and B of the Winston et al are set to pH of the present invention and alternately applied onto teeth, nitric acid or lactic acid would be produced and then teeth would be melted. In cased where the compositions A and B of Winston et al is set to pH of the present invention and are mixed before applying teeth, calcium phosphate would not be produced and teeth would be damaged.

The compositions of the present invention are formulated so that calcium phosphate and calcium phosphate is promptly formed and uptake of fluorine is increased. Therefore, when the compositions of the present invention are employed in Winston et al's method, calcium phosphate and calcium fluoride are promptly agglutinated as soon as mixed and therefore it is difficult to form calcium phosphate and calcium fluoride on teeth. Winston et al's composition is formulated in order to slowly form calcium phosphate and calcium fluoride and to form calcium phosphate and calcium fluoride as soon as applied on teeth. It differs between Winston et al and the present invention in applied method and also in control of formation of calcium phosphate and calcium fluoride. Accordingly, Winston et al or Usen et al does not teach a method for prompt formation of calcium phosphate and calcium fluoride.

Tomlinson et al specifically discloses alternate apply of the compositions A and B in example 12. While the first composition was prepared to include phosphoric acid and

sodium fluoride and have pH of 3, the second composition was prepared includes calcium nitrate and sodium hydric orthophosphate and have pH of 5. After standing, the supernatant was separated and its pH was adjusted to 7. Then, the first and second compositions are alternately applied to thereby form fluoroapatite.

However, Tomlinson et al differs from the present invention on the points that pH of the second composition is adjusted to 5 in order to form a solid of calcium hydric phosphate and then adjusted to 7 in order to stabilize a solid of calcium hydric phosphate. On the other hand, in the present invention, pH of the second composition is first adjusted to 6 to 12, none of calcium hydric phosphate is formed and then alternately applied to teeth, to thereby enable prompt formation of calcium phosphate on teeth and up take of fluorine. Moreover, Tomlinson et al's composition is prepared in two steps and needs time to form calcium hydric phosphate in the second composition, while the composition B of the present invention is prepared in one step and does not need such a time.

Accordingly, the presently claimed invention and the advantages flowing therefrom are clearly not disclosed or suggested by Winston et al, even when viewed with Tomlinson et al and Usen et al. The Examiner is again reminded that "[a] prima facie case of obviousness ... is rebuttable by proof that the claimed compounds possess unexpectedly advantageous or superior properties." *See* MPEP §2144.09 (citing *In re Paesch*, 315 F.2d 381 (C.C.P.A. 1963)). Applicants submit that the results summarized above and provided in the second Yamagishi Declaration establish that the claimed dental product possesses unexpected advantages and superior properties as compared to the products disclosed in Winston et al, even when viewed with Tomlinson et al and Usen et al.

Grabenstetter et al and Wiesel fail to compensate for the deficiencies above in the combined disclosures of Winston et al and Tomlinson et al. Specifically, Grabenstetter et al

also does not disclose the product containing fluoride in both parts. Wiesel is only cited for referring to carrier, but offers nothing with respect to the aforementioned deficiencies.

In view of the foregoing, Applicants respectfully request that these grounds of rejection be withdrawn.

Applicants submit that the present application is now in condition for allowance. Early notification of such action is earnestly solicited.

Respectfully submitted,

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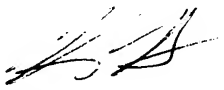

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